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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/989,577	11/20/2001	Tetsuji Okuno	4-30961A/C1	1216

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EXAMINER	
KWON, BRIAN YONG S	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 02/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/989,577	OKUNO ET AL.	
	Examiner	Art Unit	
	Brian S Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 May 2003 and 15 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-18* is/are pending in the application.

4a) Of the above claim(s) *16-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application

By Amendment filed May 23, 2003, Claims 1-10 were cancelled and Claims 11-18 were added. By Amendment filed October 15, 2003, claims 12-15 have been amended.

Applicants Response to Restriction Requirement Acknowledged

Applicants election with traverse the Group I, claims 11-15, is acknowledged. Applicants traverse the restriction requirement on the grounds that there would be no burden in searching the entire groups. This argument is not persuasive, as claimed invention would be distinctive, each from the other for the reason of the record. Furthermore, the search of the entire groups in the non-patent literature (a significant part of a through examination) would be burdensome. Therefore, the requirement is still deemed proper, and made Final. Claims 16-18 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected claims. Claims 11-15 are currently pending for prosecution on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of the specific disease conditions associated with angiogenesis (i.e., rheumatoid arthritis, osteoarthritis, myocardial infarction), does not

reasonably provide enablement for "prevention of angiogensis". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (a)). These include: 1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. All the factors have been considered with regard to the claim, with the most relevant factors discussed below.

Nature of the Invention: All rejected claims are drawn to the method of preventing angiogenesis in subjects with the administration of the instant composition.

State of the Art: The state of the art does not recognize the administration of compositions to prevent the condition as required in the instant claims. The state of the art recognizes the treatment of the symptoms of the specific disease conditions associated with angiogenesis but not their cure.

Relative Skill of Those in the Art: The relative skill of those in the cancer therapy art is high.

Predictability of the Art: The lack of significant guidance from the specification or prior art with regard to completely controlling or preventing angiogenesis in patients with the administration of the instant composition makes practicing the claimed invention unpredictable in terms of the prevention of the disease or condition.

Breadth of Claims: The scope of the instant claims is very broad due to numerous possible potential disease conditions associated with angiogenesis. The claim encompasses prevention of complex disorders that may have potential causes other than those disclosed in the specification. This may or may not be addressed by the administration of the composition

Guidance of the Specification: The guidance given by the specification on how to prevent the condition or disease is absent.

The Presence or Absence of Working Examples: Guidance for treatment of osteoarthritis, cancer (i.e., lung, breast, tongue) and metastases (i.e., lung, bone, liver) is provided.

The Amount of Experimentation Necessary: The art demonstrates treatment of the specific disease conditions associated with angiogensis in mammals, but does not teach prevention or total eradication of these conditions. Therefore, the practitioner would turn to trial and error experimentation to make/use the instant compositions for preventing memory disorders, hyperglycemia, or skin infections in mammals, without guidance from the specification or the prior art. Therefore, undue experimentation becomes the burden of the practitioner.

For examination purposes, the phrase "preventing" is interpreted as "treating" the instant conditions.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 11-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reska et al. (US 6416964).

This rejection is analogous to the original rejection.

Response to Arguments

Applicant's arguments filed May 23, 2003 have been fully considered but they are not persuasive.

Applicant's argument takes position that nothing in the reference even suggest that bisphosphonates should be administered intra-arterially or that such intra-arterial administration could result in the embolic treatment of angiogensis. Applicant alleges that the lack of such disclosure in the reference renders the present invention unobvious over the reference, especially in view of what is known about the administration of bisphosphonate generally.

The examiner disagrees. Although the approved routes of administration of bisphosphonate according to the Orange Book are generally oral and intravenous injection, what

is known in the art for the administration of bisphosphonates is far broader than what applicant alleged. The state of art also recognizes the administration of bisphosphonates in parenterally, intradermally, intranasal, inhalation, subcutaneously, vaginal, rectal or topically. It is well known in the art that parenteral injection encompasses intravenous, intraarterial, intramuscular or subcutaneous injection. Therefore, one having ordinary skill in the art would have expected that the bisphosphonates could be administered in intra-arterial injection. Those of ordinary skill in the art would have been readily optimized appropriate dosage form (i.e., intra-arterial injection) as determined by good medical practice and the clinical condition of the individual patient. Especially in light of Reszka's teaching with respect to the therapeutic utility of bisphosphonate in treating vascular restenosis or tumor growth, one having ordinary skill in the art would have been motivated to administer the claimed bisphosphonate by the intra-arterial injection with the reasonable expectation of success since intraarterial injection is known route of administration in the treatment of restenosis or tumor formation associated with angiogenesis.

Applicant has presented no evidence to establish the unexpected or unobvious nature of the claimed invention, and as such, claims 11-15 are properly rejected under 35 U.S.C. 103.

Conclusion

Applicant's amendment necessitated a new ground of rejection(s) in this Office action. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (703) 308-5377. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax number for this Group is (703) 308-4556.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Brian Kwon

ZOHREH FAY
PRIMARY EXAMINER
GROUP 1600